

Addressing Parents' Concerns About Vaccines

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Disclosures

- GlaxoSmithKline, MedImmune, Merck, sanofi pasteur, Wyeth, Novartis
- Continuing Medical Education activities
- Speaker's Bureau
- *Ad hoc* consultant
- Principal investigator

A Sampling of Anti-Vaccine Groups

National Vaccine Information Center
 The Alliance for Informed Choice in Vaccination
 Pennsylvania Parents for Vaccine Awareness
 Concerned Parents For Vaccine Safety
 Citizens for Healthcare Freedom
 Vaccine Information Resource Center
 Coalition For Informed Choice
 PAVE: People Advocating Vaccine Education
 Future Generations
 VOICE: Vaccinations- Offering Individuals Choice & Education
 Vaccination Alternatives
 Natural Immunity Information Network
 Ohio Parents for Vaccine Safety
 Healthy Alternatives
 Michigan Opposing Mandatory Vaccines

Who Are the Vaccine Protestors?

Undervaccinated	Unvaccinated
Black	White
Young, unmarried mother without college degree	Married mother with college degree
Near poverty level	Annual income >\$75,000
Live in central city	Live in states with philosophical exemptions
	Claim doctors have little influence over vaccination decisions

Smith PJ. *Pediatrics* 2004;114:187

Vaccine Programs Initiated Before 1980

Disease	Historical Peak		Most Recent	
	Cases	Deaths	Cases	Deaths
Diphtheria	30,508	3,065	0	0
Measles	763,094	552	55	0
Mumps	212,932	50	6,584	0
Pertussis	265,269	7,518	15,632	27
Poliomyelitis (acute)	42,033	2,720	0	0
Poliomyelitis (paralytic)	21,269	3,145	0	0
Rubella	488,796	24	11	0
Congenital rubella synd	20,000	2,160	1	0
Smallpox	110,672	2,510	0	0
Tetanus	601	511	41	4

Roush. *JAMA* 2007;298:2155

Vaccine Programs Initiated After 1980

Disease	Historical Peak		Most Recent	
	Cases	Deaths	Cases [†]	Deaths [†]
Hepatitis A	254,518	298	15,298	18
Hepatitis B	74,361	267	13,169	47
Hib (invasive)	>20,000	>1,000	<50	<5
Pneumo (invasive)	64,400	7,300	41,550	4,850
Varicella	5,358,595	138	612,768	19

[†]Estimates

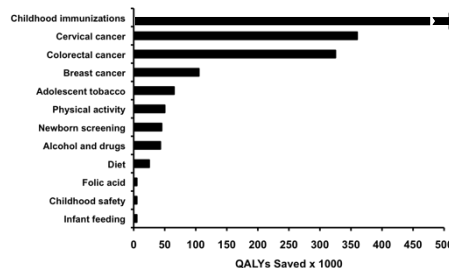
Roush. *JAMA* 2007;298:2155

Immunization Truths

1. Vaccines are good
2. Public concern about vaccines is pervasive
3. Fear of vaccines can lead to public harm
4. Vaccines are not 100% safe
5. Parents are human
6. The public doesn't understand vaccinology
7. It's all about risk perception
8. There are vaccine anti-champions
9. Questions remain
10. Parents have to make a choice

Marshall. Infect Dis Child (Suppl): Jan, 2003

Immunization Truth 1



Coffield. Am J Prev Med 2001;21:1

Immunization Truth 1

Vaccine Programs [†]	2001 Birth Cohort (N=3,803,295)		
	Cases	Deaths	Total Costs
Without	14,330,376	33,564	\$46,557 mil
With	708,372	463	\$482 mil

[†]DTaP, Hib, IPV, MMR, HepB, varicella (not included: rotavirus, HepA, PCV-7, influenza, MCV-4, HPV)

For every dollar spent, vaccine programs saved \$5 in direct medical costs and an additional \$11 in societal costs

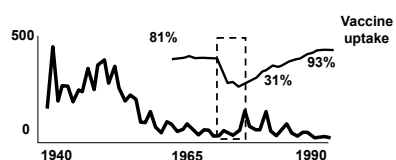
Zhou F et al. Arch Pediatr Adolesc Med 2005;159:1136-1144

Immunization Truth 2

The public is concerned about vaccination.

Immunization Truth 3

Incidence of Pertussis: England and Wales



Gangarosa. Lancet 1998;351:356

Exemptions and Pertussis Incidence

	Number of States	Adjusted Incidence Rate Ratio (95% CI)
Type of exemption		
Only religious	32	Reference
Personal belief	17	1.48 (1.03-2.13)
Exemption ease		
Difficult	19	Reference
Medium	14	1.35 (0.96-1.91)
Easy	15	1.53 (1.10-2.14)

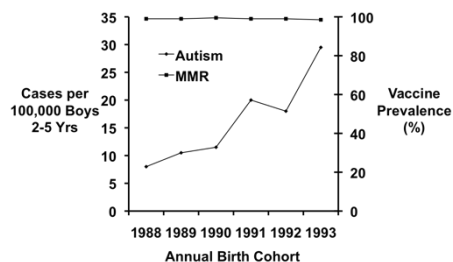
Omer SB. JAMA 2006;296:1757

Case-Control Study (Kaiser Permanente, CO)

- Cases: 156 laboratory-confirmed pertussis cases
- Controls: 595 matched controls
- Odds of vaccine refusal 23-times higher among cases than controls
- 99.5% of pertussis disease among vaccine refusers was attributable to refusal
- 11% of pertussis in the whole population was attributable to vaccine refusal

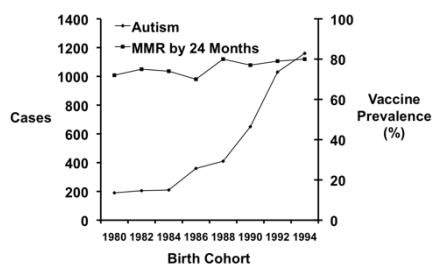
Glanz. Pediatrics 2009;123:1446

MMR and Autism: United Kingdom



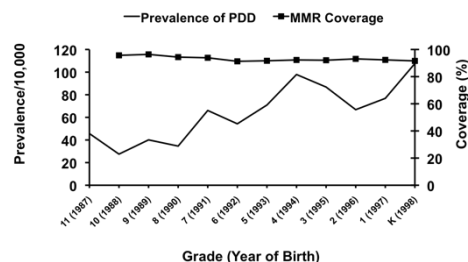
Kaye JA. BMJ 2001;322:460

MMR and Autism: California



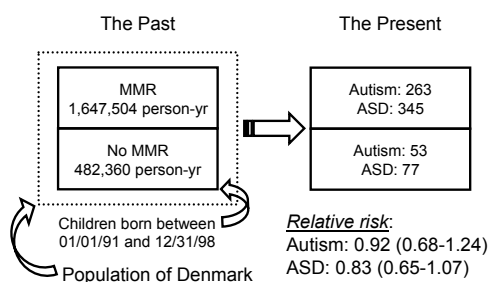
Dales L. JAMA 2001;285:1183

PDD in Montreal, Canada



Fombonne. Pediatrics 2006;118:e139

Danish Cohort Study



Madsen. N Engl J Med 2002;347:1477

Measles Virus Vaccine and Autism with Enteropathy

- Blinded search for measles RNA using RT-PCR
- 3 separate laboratories
- 25 children with autism and GI disturbances
- 13 children with GI disturbances alone

Study Group	Sex	Age at Biopsy	Time Since MMR	Where Sequences Found	Pathology
Autism	Male	4.7 yr	16 mo	Ileum	RLF
Control	Male	4.0 yr	21 mo	Ileum	RLF

RLF= reactive lymphoid follicles

Hornig. PLOS 2008;3:e3140

Consequences of Public Fear

1994
Measles eliminated

2008
Measles endemic
(again)

Jansen. Science 2003;301:804; www.eurosurveillance.org/viewarticle.aspx?articleid=18919

Measles—United States, January-July 2008

- 131 cases
 - 17 directly imported
 - 99 linked to imported cases
 - 15 link not established
 - 11% hospitalized
- 123 cases among US residents
 - 80% <20 years of age
 - 91% unvaccinated or vaccination status unknown
 - 66% of eligible individuals not vaccinated because of religious or philosophical beliefs

CDC. MMWR 2008;57:893

Invasive Hib Disease— Minnesota, 2008

Patient	Age	Syndrome	Outcome	Hib Doses
1	15 mo	Meningitis	Survived [†]	2 mo, 5 mo
2	3 yr	Pneumonia	Survived	0 [§]
3	7 mo	Meningitis	Died	0 [§]
4	5 mo	Meningitis	Survived	2 mo, 4 mo
5	20 mo	Epiglottitis	Survived	0 [§]

[†]Subsequently diagnosed with hypogammaglobulinemia

[§]Parents or guardians refused vaccination

Highest number of reported cases since 1992

CDC. MMWR 2009;58(ER);Jan 23

Immunization Truth 4: The Vaccine Safety Net

- Centers for Biologics Evaluation and Research
- Good Manufacturing Processes
- Phase I, II, and III trials
- Vaccines and Related Biological Products Advisory Committee
- FDA licensure
- ACIP, AAP and AAFP recommendations
- Mandated Phase IV studies
- Vaccine Adverse Event Reporting System (VAERS)
- Vaccine Safety DataLink (VSD)
- Clinical Immunization Safety Assessment (CISA) Centers
- Immunization Safety Review Committee
- Task Force on Safer Childhood Vaccines

Immunization Truth 5: The Power of Box “a”

		Outcome	
		Yes	No
Exposure	Yes	a	b
	No	c	d

Heuristic Thinking

- Ambiguity: a known risk is more acceptable than an unknown risk
- Do no harm: a bad outcome is more tolerable if it occurs from inaction rather than action
- Availability and representativeness: the probability that something will occur correlates with the ease with which we remember it or with similarity of circumstances
- Freeloading: herd immunity will protect my child
- Compression: rare risks are overestimated and common risks are underestimated

Evans. Risk Comm and Vac. Natl Acad Press, 1997; Ball. Pediatrics 1998;101:453

Immunization Truth 6

Age > Vaccine?	Birth	1 mo	2 mos	4 mos	6 mos	12 mos	15 mos	18 mos	24 mos	4-6 yrs	11-12 yrs	14-18 yrs
Diphtheria, Tetanus, Pertussis			DTP	DTP	DTP			DTP		DTP		Td
Polio			OPV	OPV	(OPV)			OPV		OPV		
Measles, Mumps, Rubella							MMR					

Antigen Burden

Vaccine	1960	1980	2000	2007
Smallpox	200			
Diphtheria	1	1	1	1
Tetanus	1	1	1	1
Pertussis	3000	3000	5	5
Polio	15	15	15	15
Measles		10	10	10
Mumps		9	9	9
Rubella		5	5	5
Hib			2	2
Varicella			69	69
PCV7			8	8
HepB			1	1
HepA				4
HPV4				4
Rotavirus				5
MCV4				5
Influenza				12
Total	3217	3041	126	156

Offit. Pediatrics 2002;109:124 and Marshall. The Vaccine Handbook. PCI Books: 2008

Dr. Bob's Alternative Vaccine Schedule

	0	1	2	4	6	12	15	18	19-23	2-3	4-6
HepB											
Rota											
DTaP											
Hib											
PCV7											
IPV											
Flu											
Measles											
Varicella											
HepA											

Sears. The Vaccine Book. Little Brown & Co. 2007

Analysis of Dr. Bob's Alternative Schedule

Argument	The Truth
Doctors do not understand vaccines. Parents can educate themselves to know more than doctors.	Doctors may not always review the primary data, but the advisory committees that do are composed of experts whose record has been spot-on.
Government and pharmaceutical companies conspire to misrepresent data. Vaccinations should be optional.	There is no evidence of conspiracy. Mandates have dramatically reduced hospitalizations and deaths. States that allow personal belief exemptions have higher rates of disease.
Vaccine-preventable diseases are not that serious and are often not seen in practice.	Vaccine-preventable diseases are serious and can result in death. Anecdotal experience in practice does not trump national surveillance data.
Unvaccinated children are protected by herd immunity.	Measles has spread in communities where parents chose not to immunize their children.

Offit. Pediatrics 2009;123:e164

Analysis of Dr. Bob's Alternative Schedule

Argument	The Truth
Natural immunity is better than vaccine-induced immunity.	The cost of natural immunity is the risk of serious disease or death.
Vaccines cause chronic diseases and may contain toxic ingredients.	A clear body of scientific evidence refutes these claims.
Vaccines are not adequately tested for safety.	Vaccines are among the most thoroughly tested pharmaceuticals. The post-licensure safety net is robust.
Vaccines are recommended for protection of the public at large, not individuals.	Every individual benefits from receiving vaccines— they become immune to the disease and, as long as others are immunized, they have less chance of exposure.
Parents' fears should be indulged by offering alternative schedules.	Parents' fears should be assuaged by explaining the scientific findings.

Offit. Pediatrics 2009;123:e164

Analysis of Dr. Bob's Alternative Schedule

Argument	The Truth
Reports in VAERS and language in the Package Insert (PI) constitute accurate profiles of vaccine side effects.	VAERS reports do not establish causality and the PI lists any reported events, whether causally related or not.
There is a middle ground between causality and coincidence.	This logic is flawed— either vaccines do or don't cause certain adverse events.
Science fails because it cannot prove there is no connection between vaccines and certain adverse events.	Science doesn't work that way— one can only reject or fail to reject the null hypothesis.

Offit. Pediatrics 2009;123:e164

Immunization Truth 7: Risk Perception

You're invited to a chickenpox party!

New York Post- 1/11/09

Immunization Truth 8: The New McCarthyism

- "I have a family history of genetic vulnerability that my kid can't detox vaccines."
- "They say the mercury (thimerosal...) is gone, but it's still in there!"
- "...no wheat, no dairy, because his system can't break them down... it turns them into an opiate making them stoned or drunk...detoxing and occasionally antifungal medicines."
- "It's the pediatrician's fault! Not my fault!"
- "...I'm on an airplane and the pilot comes out to talk to me because his kid is autistic."

US Weekly. Oct 27, 2008

Cohort Studies of Thimerosal Exposure

Study	Location	Database	Inclusion/Exclusion Criteria	Diagnoses Precisely Defined	Outcome Measures Validated	Appropriate Calculation of Thimerosal Exposure	Control for Bias
Geier 2003	USA	VAERS	No	No	No	No	No
Geier 2003	USA	VAERS DOE	No	No	No	No	No
Geier 2003	USA	VAERS DOE	No	No	No	No	No
Andrews 2004	UK	National Statistics	Yes	Yes	Yes	Yes	Yes
Heron 2004	UK	Avon Long Study	Yes	No	No	Yes	Yes
Hvid 2003	Denmark	National Registries	Yes	Yes	No	Yes	Yes
Vonstratten 2003	USA	HMOs	Yes	Yes	Yes	Yes	No

Parker. Pediatrics 2004;114:793

Dr. Mark Geier and Mr. David Geier

- **Mark Geier, M.D., Ph.D.**
 - President of The Genetic Centers of America
 - Institute for Chronic Illness
 - Doctorate in Genetics
 - Board-certified in Medical Genetics and Forensic Medicine
- **David Geier: President of MedCon (legal consulting firm)**

Deer. BMJ 2007;334:666

Court Opinions About Dr. Geier

- "...Dr. Geier has made a profession of testifying in matters to which his professional background...is unrelated"
 - Federal Judge, Ormechea v. Secretary of DHHS, No. 90-1683V, slip op. at 20, 24, [Fed. Cl. 1992]
- "...affidavit was seriously intellectually dishonest."
 - Special Master, Marascalco v. DHHS, No. 90-1571V [Fed. Cl. 1993]
- "None of Dr. Geier's research aimed at establishing a link between thimerosal and autism, moreover, is based upon sound methodology."
 - J. Battaglia, Blackwell v. Wyeth, et al. Maryland Court of Appeals; May 7, 2009

Vaccine Adverse Event Reporting System

- Post-marketing surveillance system
- Mandatory reporting by health care providers
 - Events listed as contraindications
 - Events listed in the Reportable Events Table
- Voluntary reporting: any event by any one
- Intent: *hypothesis generation* not *hypothesis testing*

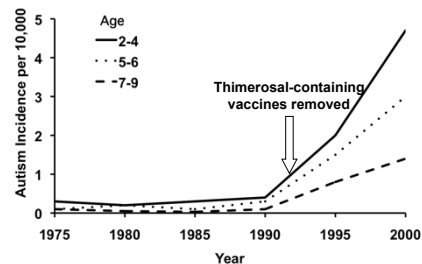
Offit, in Marshall. The Vaccine Handbook. Lippincott Williams & Wilkins, 2004

VAERS Only Contains Box "a"

		Outcome	
		Yes	No
Exposure	Yes	a	b
	No	c	d

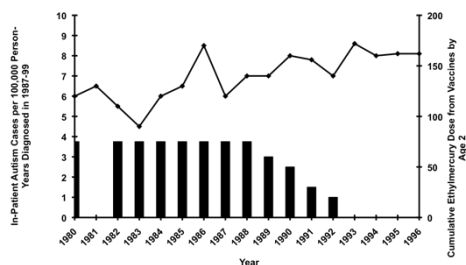
87% of all thimerosal-related VAERS reports in 2002 were made by lawyers

Danish Population-Based Study



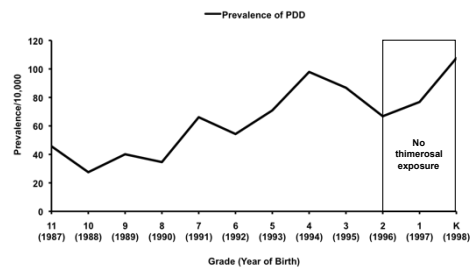
Madsen. *Pediatrics* 2003;112:604

Swedish Population-Based Study



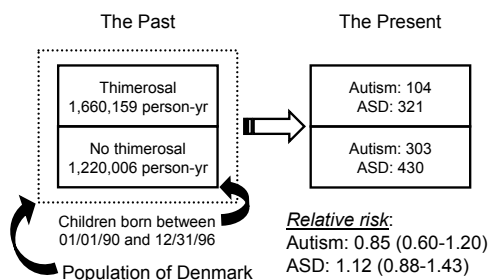
Stehr-Green. *Am J Prev Med* 2003;25:101

PDD in Montreal, Canada



Fombonne. *Pediatrics* 2006;118:e139

Danish Cohort Study



Hviid. *JAMA* 2003;290:1763

Thimerosal Status of Current Vaccines

Vaccine	Trade Name	Manufacturer	Status
Diphtheria, tetanus, pertussis	Infanrix DAPTACEL Triptedia	GlaxoSmithKline Aventis Pasteur Aventis Pasteur	Free Free Free <0.3 mcg/0.5mL
PCV-7	Prevnar	Wyeth	Free
Polio	IPOL	Aventis Pasteur	Free
Hepatitis B	RECOMBIVAX HB Engerix-B	Merck GlaxoSmithKline	Free Free <0.5 mcg/0.5mL
Hib conjugate	ActHIB PedvaxiHB	Aventis Pasteur Merck	Free Free (single dose)
Hib/Hepatitis B	COMVAX	Merck	Free
MMR	M-M-R ₂	Merck	Free
Varicella	VARIVAX	Merck	Free
DTaP/Hep-B/IPV	Pediaris	GlaxoSmithKline	<0.0125 mcg/0.5 mL
Influenza	Fluzone T-free	sanofi pasteur	Free
	Fluvirin P-free	Chiron/Evans	<1.0 mcg/0.5 mL
	Flumist	MedImmune	Free
Hepatitis A	VAQTA	Merck	Free
	Havrix	GlaxoSmithKline	Free

www.fda.gov/cber/vaccine/thimerosal.htm#t1 (accessed 07/30/06)

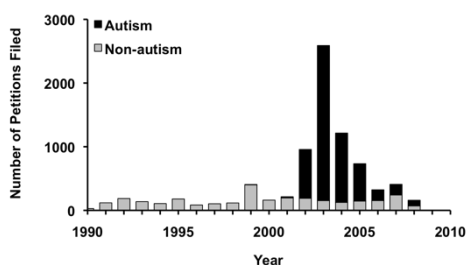
Vaccine Injury Compensation Program

- National Childhood Vaccine Injury Act (P.L. 99-660) enacted in 1986
- No-fault alternative to tort system for claims related to mandated childhood vaccines
- Jointly administered by DHHS, U.S. Court of Federal Claims, and Department of Justice
- Funded by excise tax on vaccines
- Claimants must first seek remedy through VICP
- Claims either settled or referred to Special Masters for adjudication

Compensable Claims

- Vaccine Injury Table: presumption of causation
- Injuries not listed
 - Preponderance of the evidence
 - Biologic plausibility
 - Not necessary to establish causation in the scientific sense

VICP Petitions



http://www.hrsa.gov/vaccinecompensation/statistics_report.htm

Omnibus Autism Proceedings

- Theories of general causation
 - MMR and thimerosal-containing vaccines combine to cause autism
 - Thimerosal-containing vaccines cause autism
 - MMR causes autism (dropped)
- Three test cases per theory

Magnitude of The Vaccine Court Hearings

- Typical vaccine case
 - 10 medical articles
 - 2-6 experts
- Omnibus Proceedings for Theory 1
 - 5,000 pages of transcript
 - >700 pages of post-Hearing briefs
 - 939 medical articles
 - 50 expert reports
 - Testimony of 28 experts

US Court of Federal Claims. <http://www.uscfc.uscourts.gov/node/5026> (accessed 02/18/09)

Cedillo Case

"... the evidence was overwhelmingly contrary to the petitioners' contentions. The expert witnesses presented by the respondent were far better qualified, far more experienced, and far more persuasive than the petitioners' experts, concerning most of the key points. The numerous medical studies concerning these issues, performed by medical scientists worldwide, have come down strongly against the petitioners' contentions."

Special Master Hastings. Office of Special Masters No. 98-916V. 02/12/09

Hazlehurst Case

"The weight of the presented evidence that is scientifically reliable and methodologically sound does not support petitioners' claim."

Special Master Campbell-Smith. Office of Special Masters No. 03-654V. 02/12/09

Snyder Case

"... it was abundantly clear that petitioners' theories of causation were speculative and unpersuasive... petitioners could not reliably demonstrate the presence of a persistent measles virus in Colten's central nervous system... failed to establish that measles virus can cause autism or that it did so in Colten... failed to demonstrate that amount of ethylmercury in TCVs causes immune system suppression or dysregulation... failed to show that Colten's immune system was dysregulated."

Special Master Vowell. Office of Special Masters No. 01-162V. 02/12/09

Immunization Truth 9: Questions

- Which challenges deserve scientific investigation?
- How can we respond without the perception of conflict of interest?
- How do families differ in medical orientation?
- Should families who refuse to vaccinate be fired?

AMA Code of Ethics

- E-8.115: Physicians have an obligation to support continuity of care for their patients. While *physicians have the option of withdrawing from a case*, they cannot do so without giving notice to the patient, the relatives, or responsible friends sufficiently long in advance of the withdrawal to permit another medical attendant to be secured.
- E-10.05: ...it may be ethically permissible for physicians to decline a potential patient when...*the treatment request is known to be scientifically invalid*, has no medical indication, and offers no possible benefit to the patient

www.ama-assn.org/ama/pub/category/8288.html (accessed 03/18/04)

The All Star Pediatrics Manifesto

"...by not vaccinating your child you are taking selfish advantage of thousands of others who do vaccinate their children, which decreases the likelihood that your child will contract one of these diseases. We feel such an attitude to be self-centered and unacceptable."

"...if you should absolutely refuse to vaccinate your child despite all our efforts, we will ask you to find another health care provider who shares your views. We do not keep a list of such providers, nor would we recommend any such physician. Please recognize that by not vaccinating you are putting your child at unnecessary risk for life-threatening illness and disability, and even death."

Dyer. AAP News: May 2008 (www.aap.org/securemoc/immunizations/allstarpediatrics.doc)

Immunization Truth 10: Parental Choice

Don't vaccinate	Vaccinate
Listen to discredited "scientists"	Listen to robust science
Listen to "advocacy groups"	Listen to authoritative bodies
Listen to celebrities	Listen to providers
Vulnerability to disease	Protection from disease